Pneumococcal carriage and disease in Native Americans in the era of routine use of PCV13

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ACIP Meeting: June 21, 2018

Disclosures

- Research grants from Merck, Pfizer, GSK

Overview

- Pneumococcal Carriage
  - Southwest US
  - Alaska Native (CDC/AIP)
- Invasive Pneumococcal Disease
  - Southwest US
  - Alaska Native (CDC/AIP)
- Adult Community Acquired Pneumonia
  - Southwest US

PCV13 coverage

- Children
  - Indian Health Service (IHS) immunization registry
    - 3-4 mos (1 dose): ~85%
    - 7-15 mos (3 doses): ~80%
    - 24-27 mos (4 doses): ~85%
- Adults ≥65 years
  - CAIH study participants: ~60-80% in 2015-2017
  - Alaska VacTrAK: 13% in 2015, 24% in 2016

https://www.ihs.gov/NonMedicalPrograms/ihpes/Immunizations/index.cfm?module=immunizations&option=reports

Alaska data courtesy of Mike Bruce CDC/AIP

Pneumococcal Carriage

Funding for CAIH study: Clinical Research Collaboration with Pfizer, Inc.

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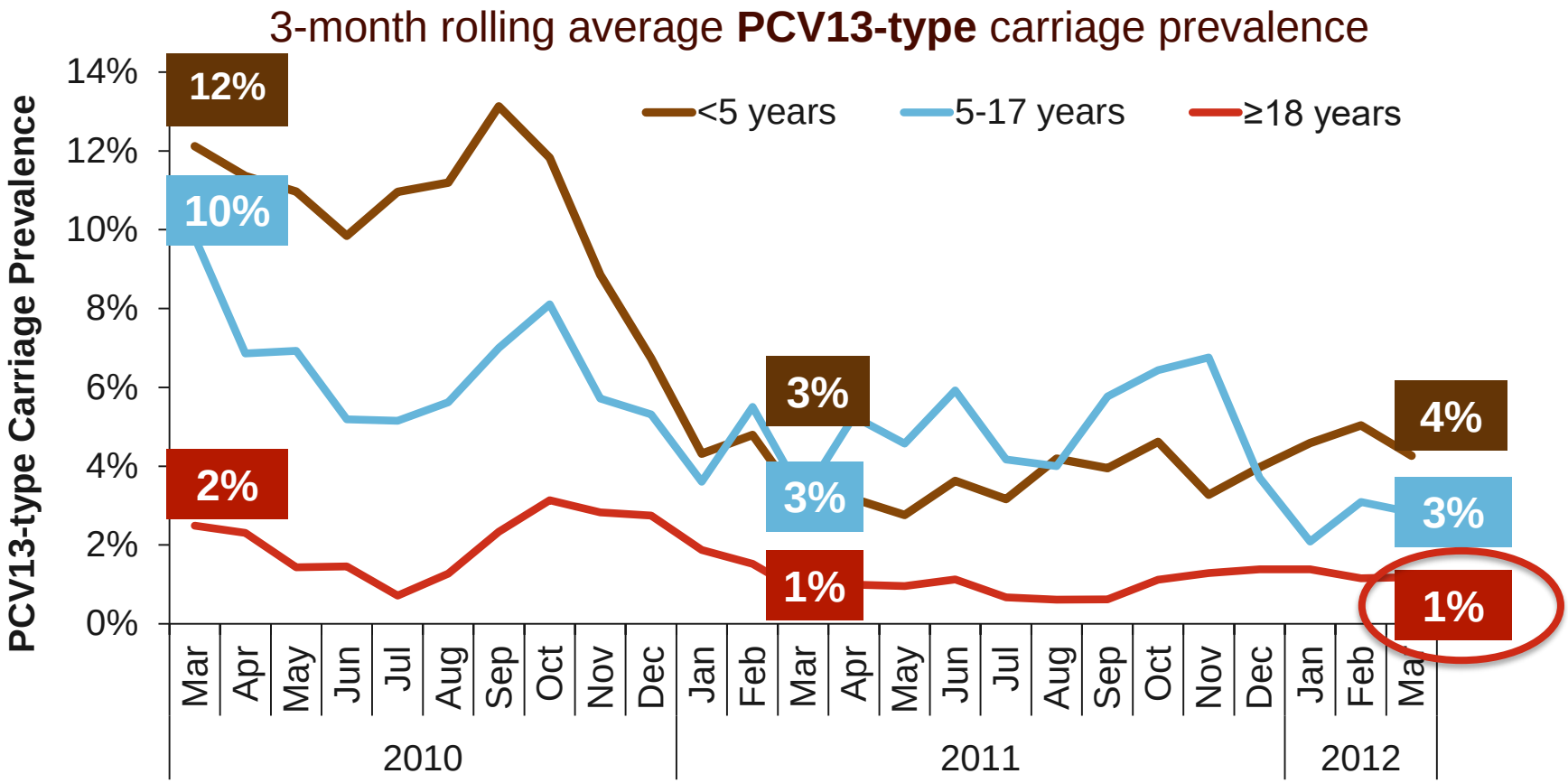
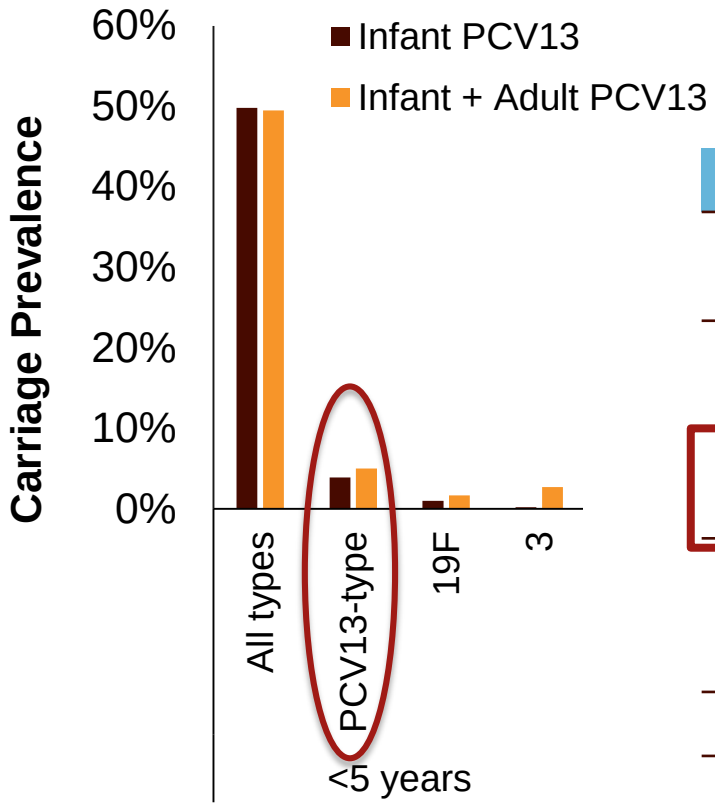
Nasopharyngeal carriage: Early infant PCV13 era (2010-2012)



Convenience sample; household based
NP flocked swab with broth-enrichment culture
Serotyping by latex agglutination and Quellung

Grant et al, *Pediatr Infect Dis J* 2016;35:907–914

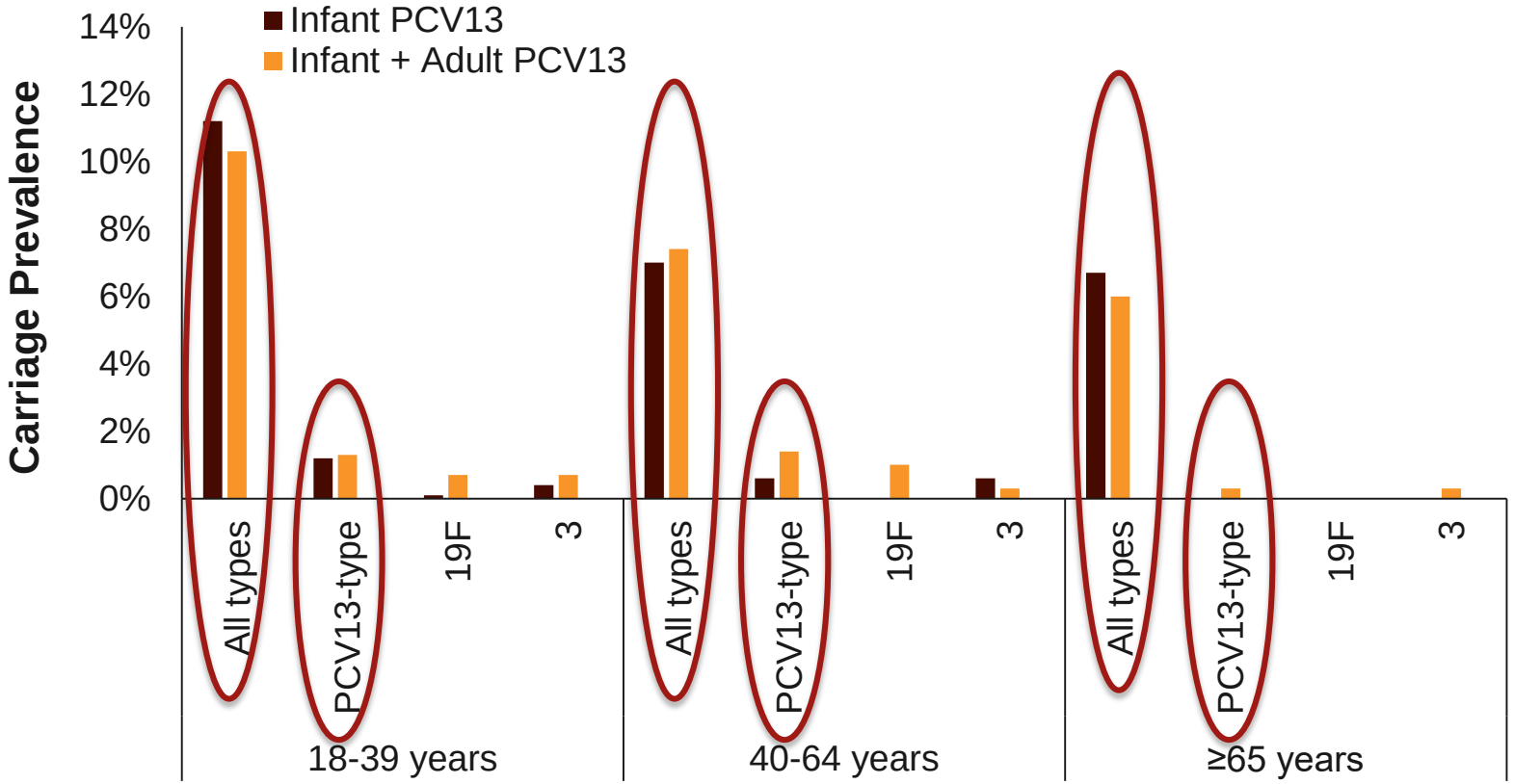
Nasopharyngeal carriage: Infant PCV13 (2011-2012) vs Infant + Adult PCV13 eras (2015-2017)



Infant PCV13	N=1365
Infant + Adult	N=600

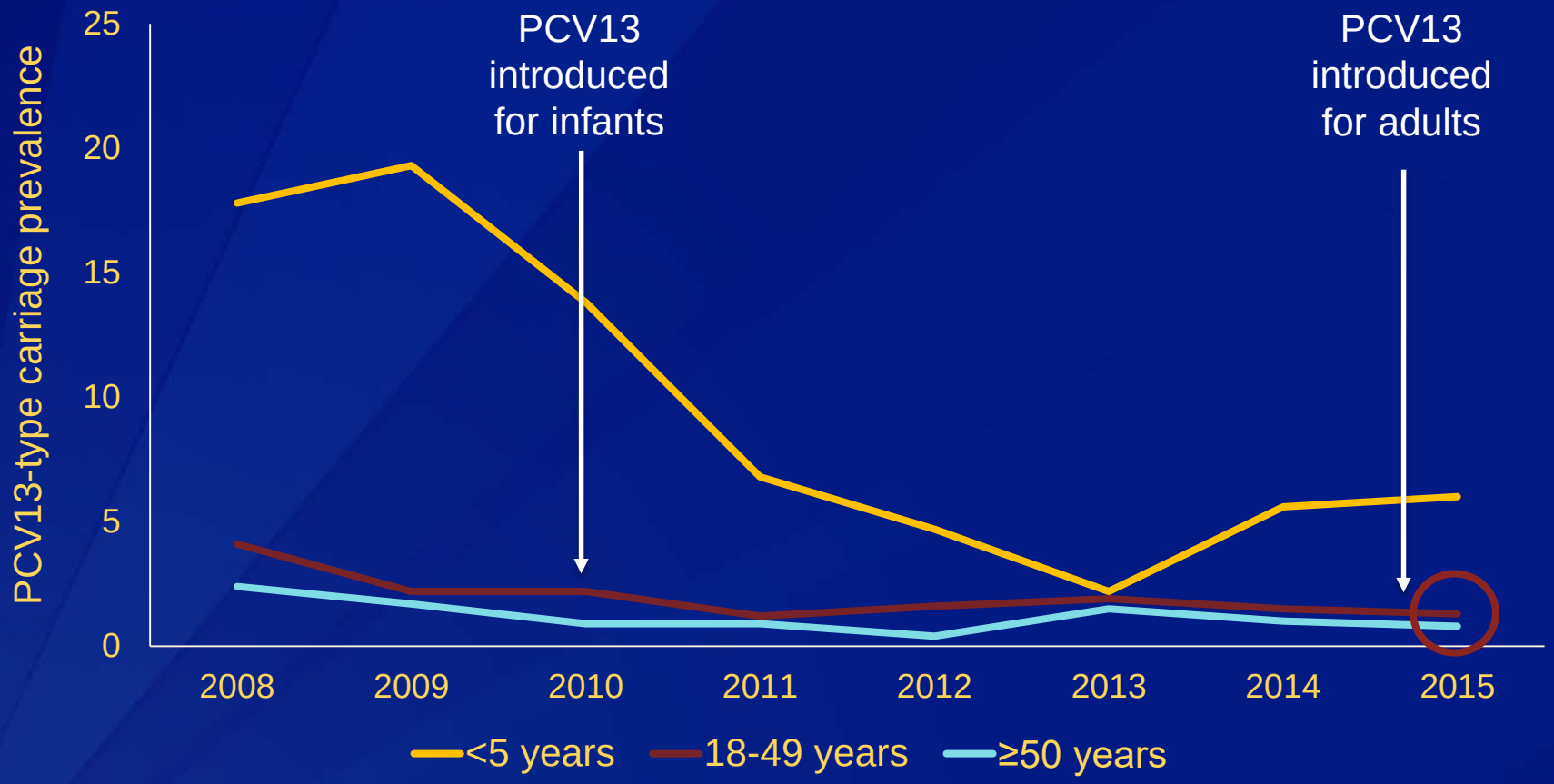
Characteristic	Infant PCV13	Infant+Adult PCV13
Design	Convenience, **household based**	Convenience
Population	Native American; **all ages**	Native American; <5yrs and adults
Median age (IQR), adults	**27 years** (22, 34)	**53 years** (33, 68)
Specimen	NP flocked swab stored in STGG	NP flocked swab stored in STGG; **OP** swab in adults
Culture	Broth enrichment	Broth enrichment
Serotyping	**Quellung**	**Sequetyping**

Nasopharyngeal carriage: Infant PCV13 (2011-2012) vs Infant+Adult PCV13 eras (2015-2017)



Infant PCV13	N=1020	N=157	N=45
Infant + Adult	N=301	N=296	N=300

PCV13-type Nasopharyngeal Carriage in Alaska Native People in Rural Alaska



Slide courtesy of Mike Bruce, CDC/Arctic Investigations Program

Conclusions

- PCV13-type pneumococcal carriage in adults was very low following infant PCV13 introduction and remains low

Invasive Pneumococcal Disease

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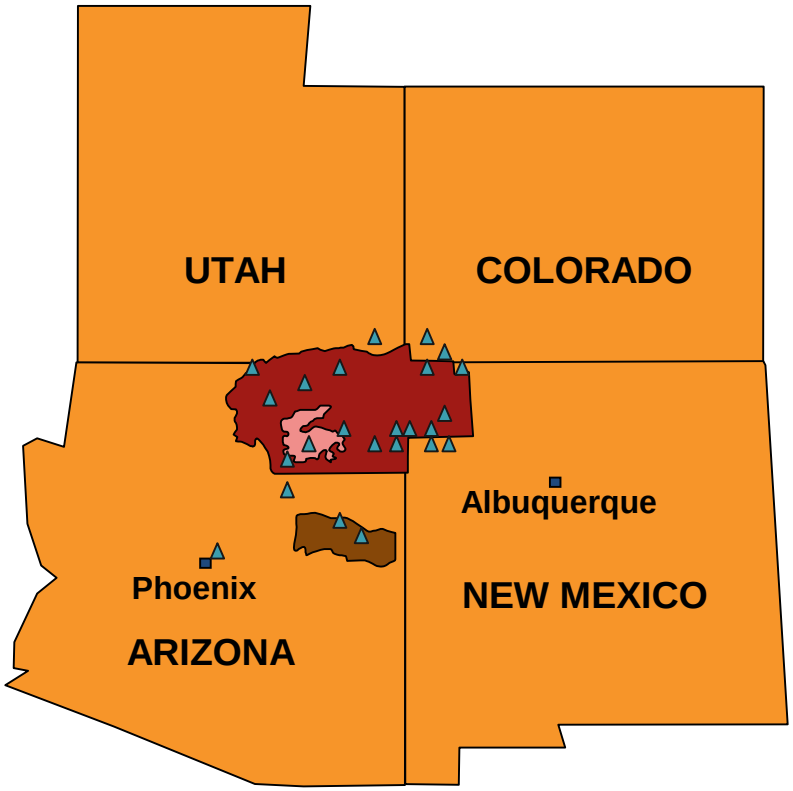
CAIH Active Bacterial Surveillance

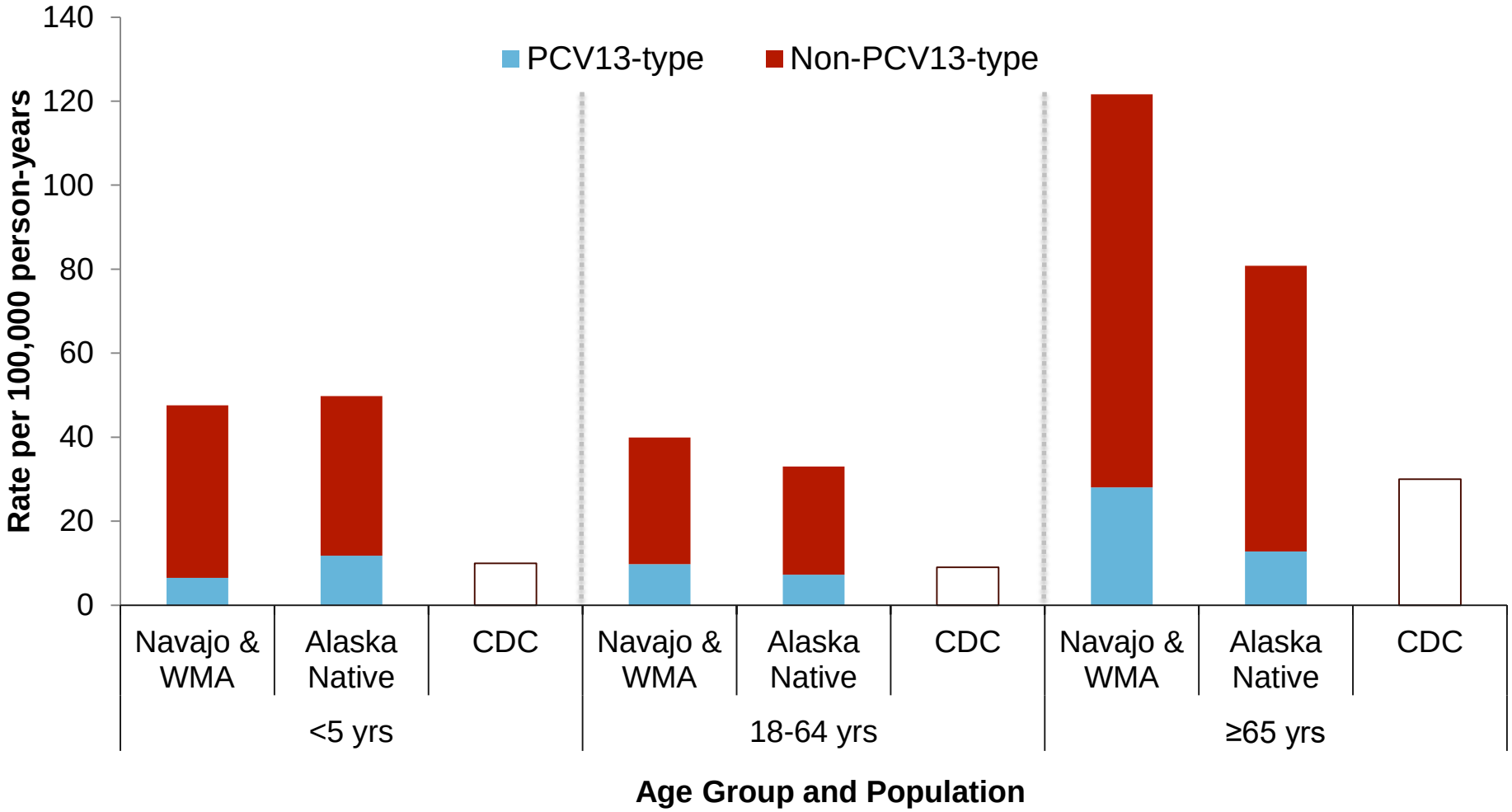


Key:

- Navajo Nation
- White Mountain Apache
- Hopi
- Surveillance Laboratory

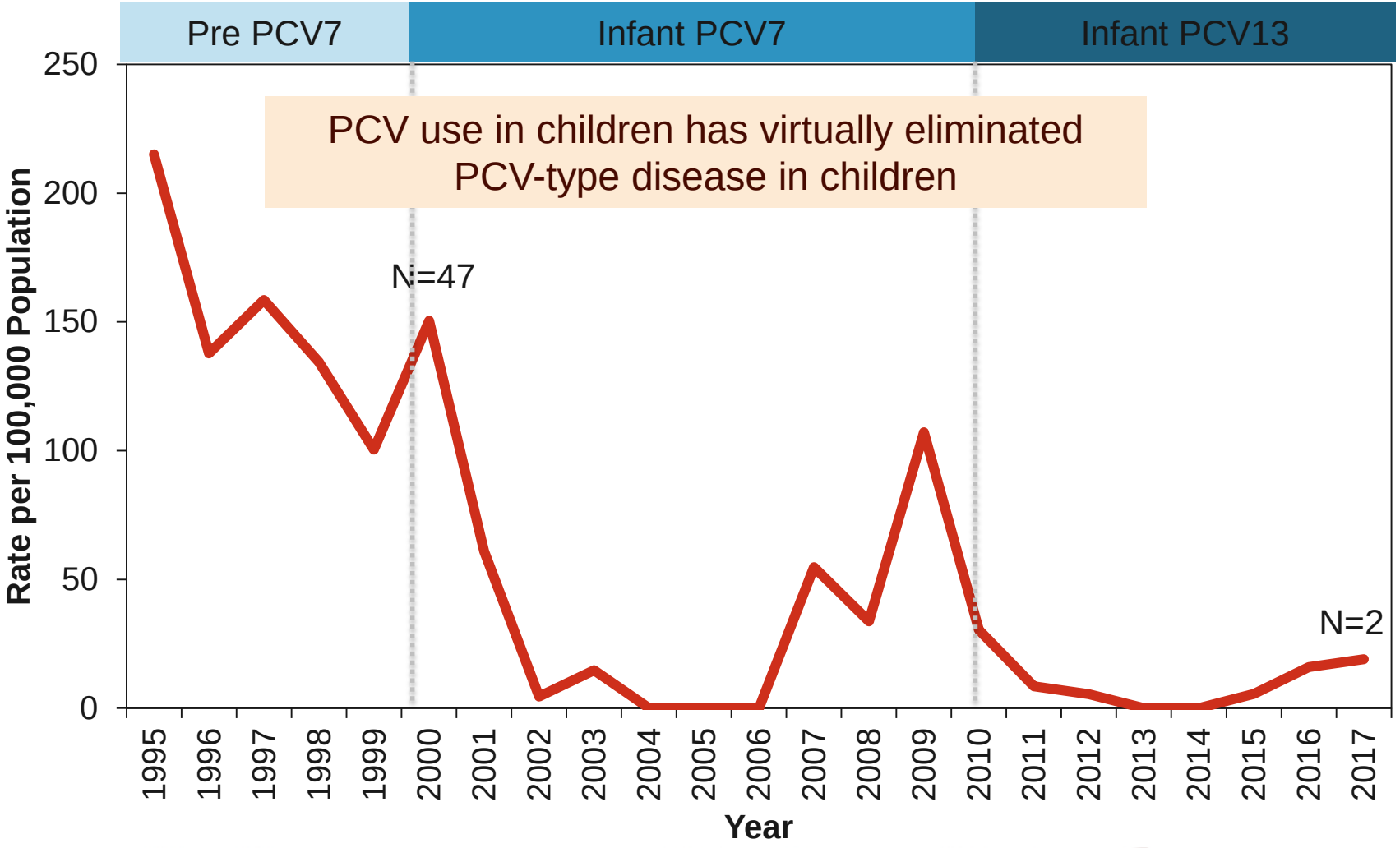
- ***Actively contact*** *laboratory facilities*
  - *Navajo* – 21 labs
  - *White Mountain Apache* – 3 labs
- ***Identify*** pneumococcal isolates that meet inclusion criteria
  - Serotyped at CDC/Arctic Investigations Program
- *Conduct* ***chart reviews***

All Serotype IPD: Native Americans, Alaska Natives and General US, 2011-2015

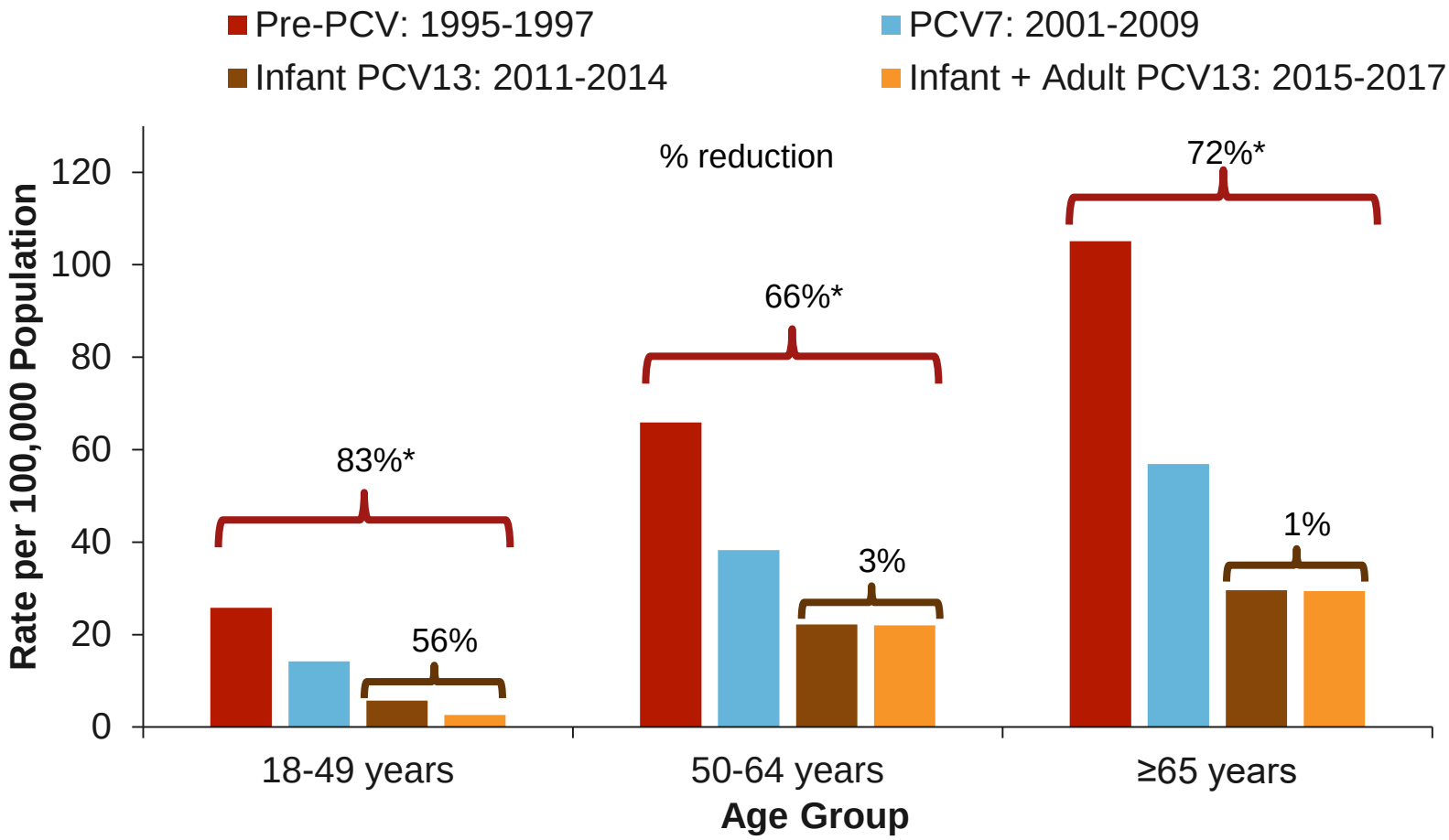


Navajo/White Mountain Apache data from CAIH ABS; Alaska Native data courtesy of CDC/AIP; CDC data from ABCs surveillance reports

PCV13-type IPD: Navajo children <5 years, 1995-2017

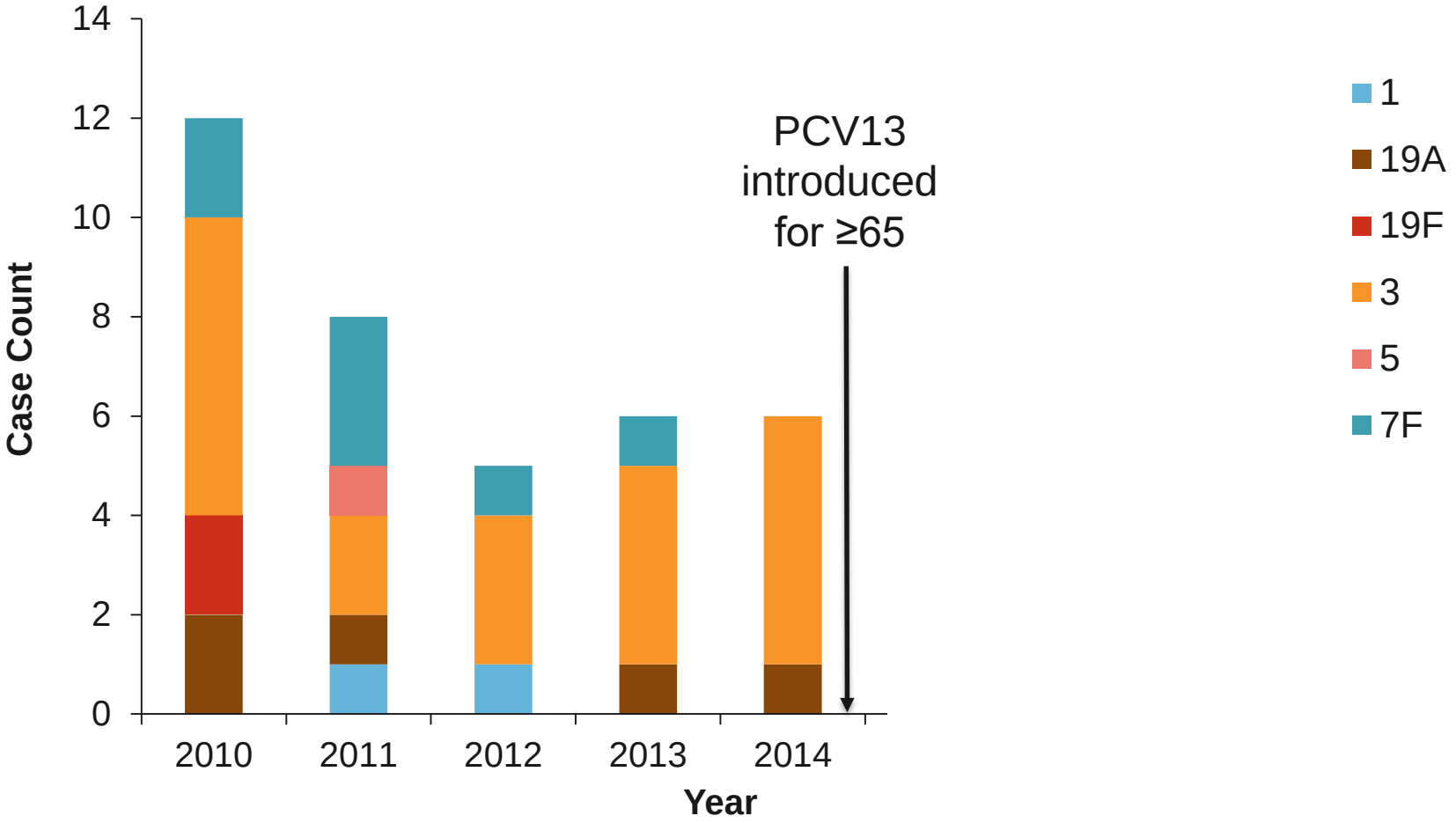


PCV13-type IPD incidence pre- vs. post-PCV, Navajo adults ≥18 years

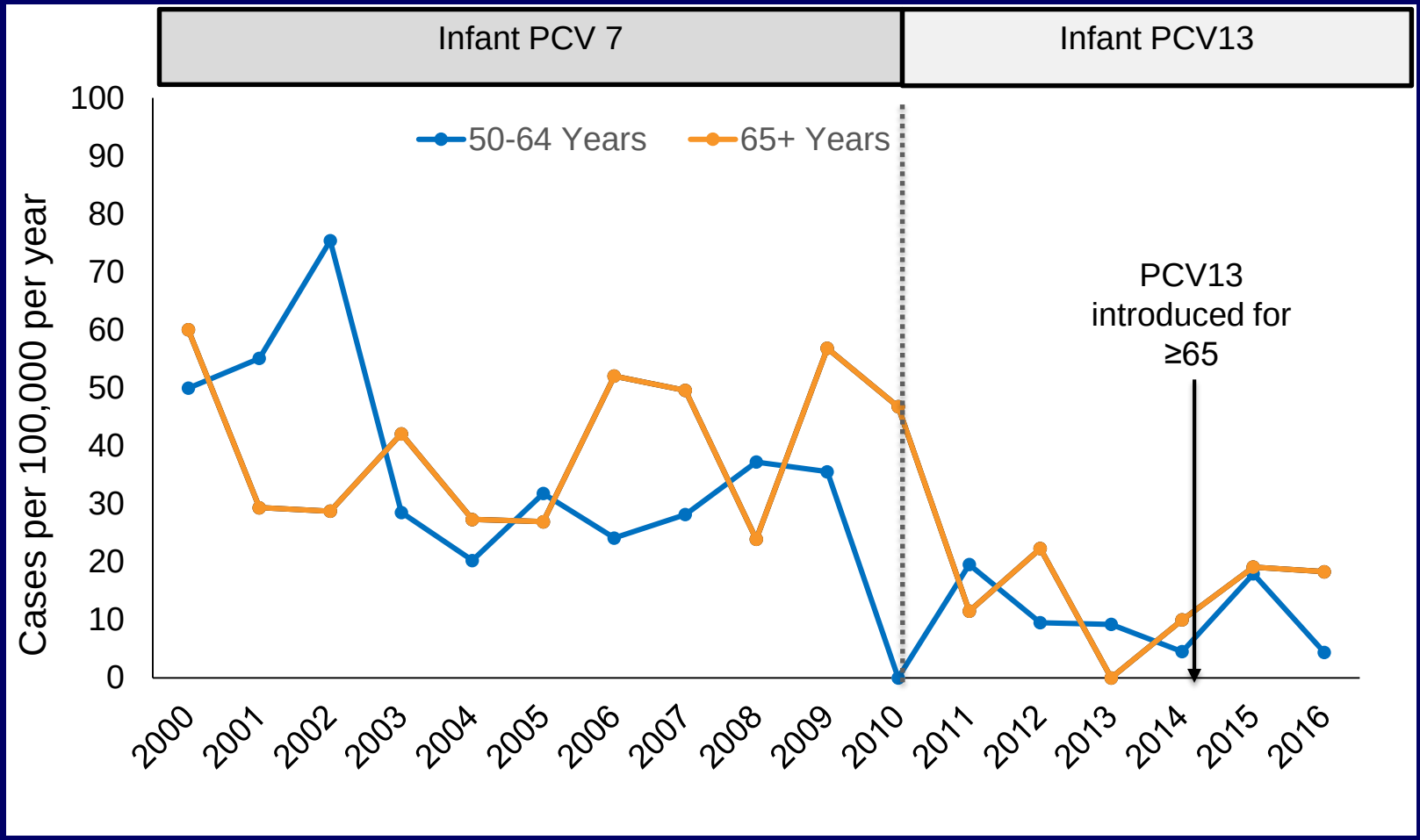


*Statistically significant

PCV13-type IPD serotype distribution: adults **≥65 years**, Navajo, 2010-2017

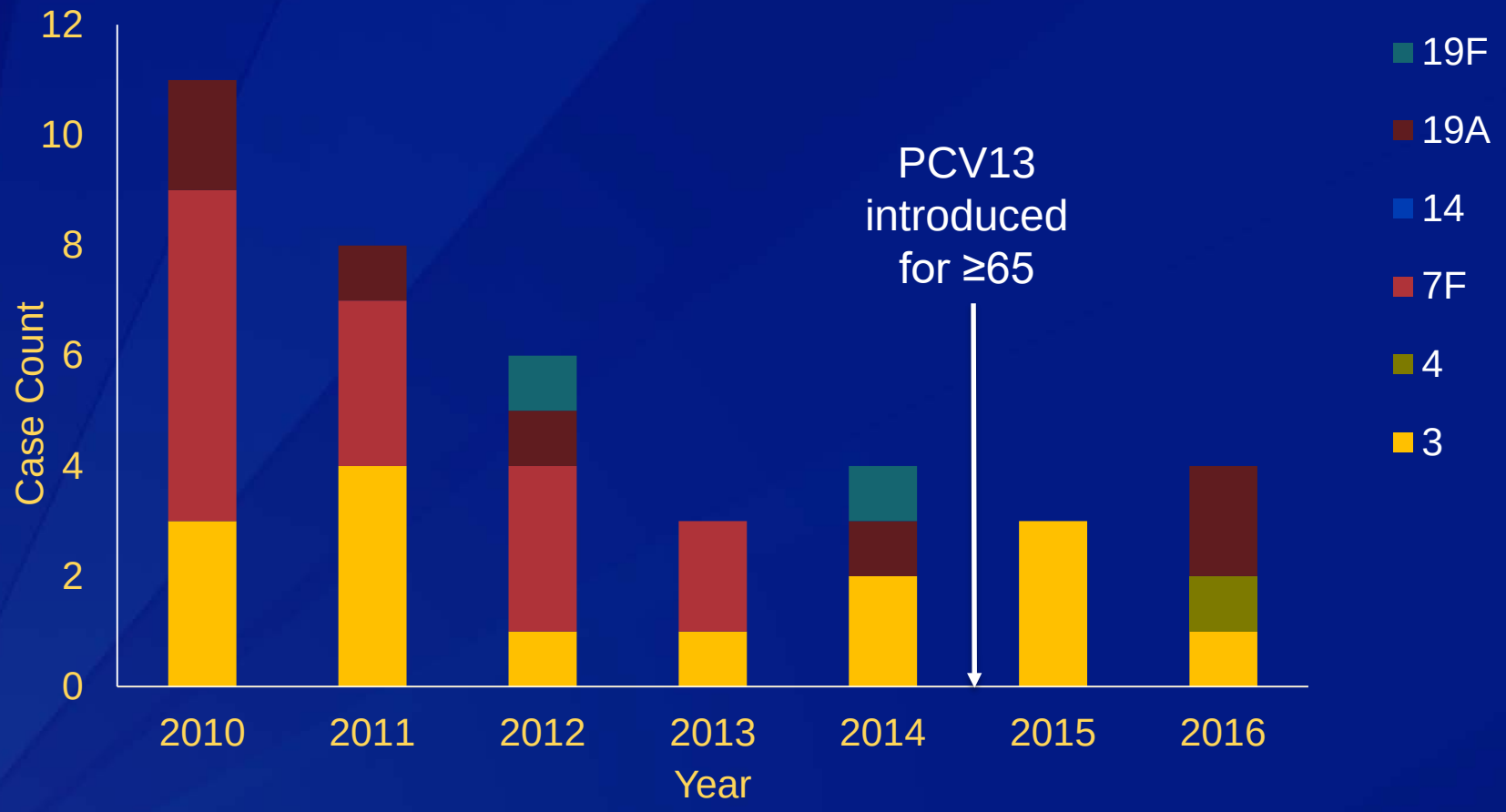


PCV13-type IPD: Alaska Native adults ≥50 years, 2000-2016



Slide courtesy of Mike Bruce, CDC/Arctic Investigations Program

PCV13-type IPD distribution: ≥65 years Alaska, 2010-2016



Slide courtesy of Mike Bruce, CDC/Arctic Investigations Program

Conclusions

- PCV13-type NP carriage in adults was very low prior to use of PCV13 in older adults and remains low
- Substantial indirect effects had been achieved by 2014-2015, leaving little opportunity to assess impact of PCV13 in ≥65 year olds on carriage or IPD

Native American Adult Pneumonia Etiology Study, March 2016 – March 2018

Funding: Clinical Research Collaboration with Pfizer, Inc.

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Study activities

- Cases identified through surveillance at 5 IHS hospitals
  - Native American adult hospitalized with community acquired pneumonia (CAP)
  - Two or more clinical signs/symptoms at least one of which is respiratory
- Controls identified within 2 weeks of case
  - Age-matched, convenience sample
  - Without CAP or suspicion of CAP
  - 1 control for every 2 cases

- Obtain informed consent

- Collect specimens

- Administer questionnaire and perform chart review

Laboratory data

		Assay	Test performed by
	Blood	Culture, per clinical team	Indian Health Service
		Serum for biomarkers*	To be determined
	Urine	SS-UAD for 24 serotypes*	Pfizer
		S. pneumoniae BinaxNOW*	Pfizer
	NP/OP swab	Multiplex PCR*	JHU/CDC (pending)
		*lyt*A PCR, serotype-specific PCR*	Pfizer (pending)
	Sputum	Culture, per clinical team	Indian Health Service
	CXR	Radiography, per clinical team	Indian Health Service

*available for cases and controls

SSUAD

- SSUAD 1
  - PCV13 serotypes, clinically validated and FDA approved for research
- SSUAD 2
  - Serotypes 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F
  - Well-characterized; not clinically validated at start of study
- Population-specific thresholds
  - SSUAD results from 400 Native American adults in the study community used to inform established thresholds → reset the positivity cut-off for serotype 14

Pride et al, Clin Vaccine Immunol 2012; 19:1131–1141
Pride et al, Clin Vaccine Immunol 2017; 24:e00239-17

Demographic characteristics

Characteristic		CXR+ Cases N=355 n (%)	Controls N=269 n (%)	P-value
Female		193 (54.4)	200 (74.4)	<0.001
Median age, years (IQR)		66 (51, 79)	68 (54, 79)	
Age group (years)				
	18-49	78 (22.0)	54 (20.1)	0.93
	50-64	89 (25.1)	67 (24.9)	
	65-79	107 (30.1)	82 (30.5)	
	≥80	81 (22.8)	66 (24.5)	
Smoker resides in household		22 (6.2)	5 (1.9)	<0.01
Primary fuel for cooking is wood		13 (2.8)	10 (3.7)	0.97
Household has piped water[1]		289 (98.6)	234 (99.2)	0.58
Household has flush toilet		292 (82.2)	236 (87.7)	0.10

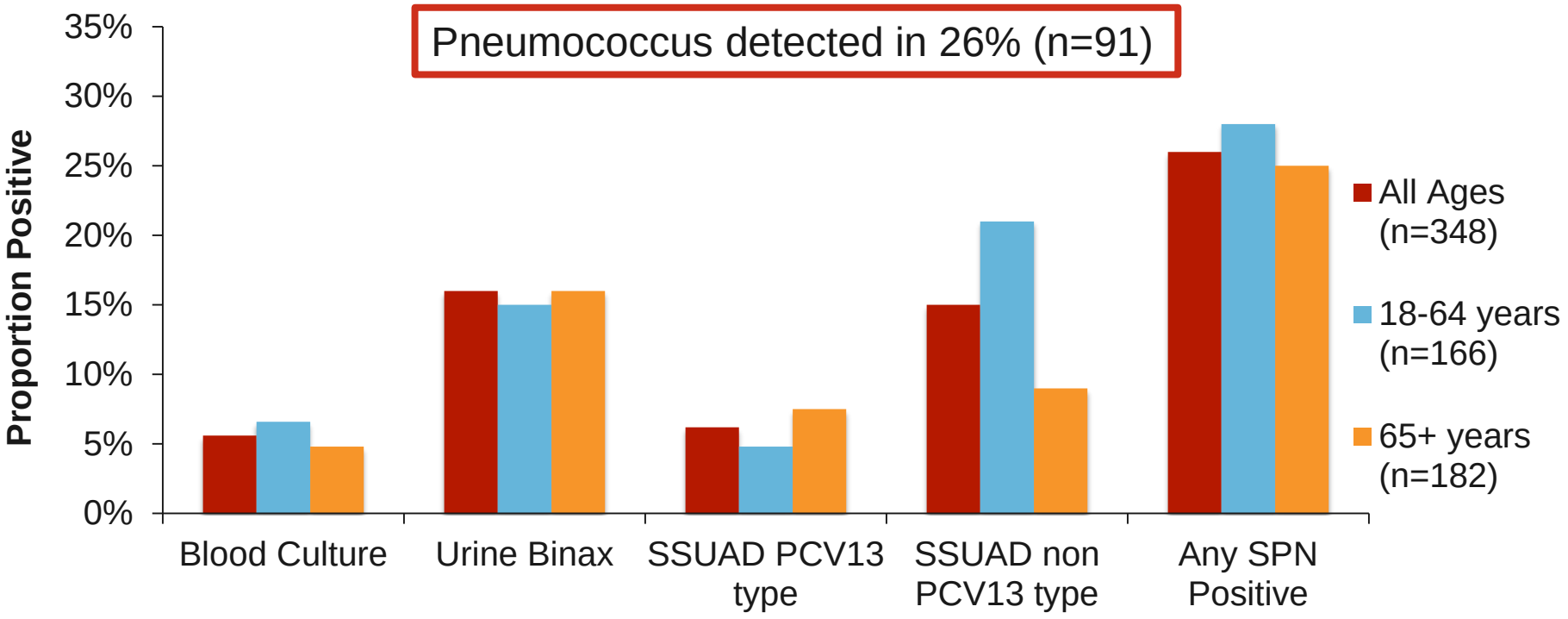
[1]Denominator includes 293 cases and 236 controls with available data.

Clinical characteristics

Characteristic	CXR+ Cases N=355 n (%)	Controls N=269 n (%)	P-value
Duration of illness* - days median (IQR)	3 (2, 7)	n/a	
Any underlying condition	335 (94.4)	218 (81.0)	<0.001
Chronic lung disease	39 (11.0)	5 (1.9)	<0.001
Chronic heart disease	49 (13.8)	10 (3.7)	<0.001
Diabetes	161 (45.4)	97 (36.1)	0.04
Malignancy	45 (12.7)	12 (4.5)	<0.001
No. of chronic conditions – median (IQR)	1 (0, 4)	1 (0, 3)	0.31
Outcome, discharged alive – n (%)	349 (98.3)	n/a	
Immunization history			
<65 years	n (%)	n (%)	
PPV23 ever	110 (65.9)	58 (47.9)	<0.01
PCV13 ever	13 (7.8)	4 (3.3)	0.11
≥65 years	n (%)	n (%)	
PPV23 ever	172 (91.5)	144 (97.3)	0.03
PCV13 ever	152 (80.8)	120 (81.1)	0.96

*from illness onset to hospital presentation

S. pneumoniae positivity by test CXR+ cases with any pneumococcal test (N=348)



SSUAD increased the detection of pneumococcal cases by **57%**.

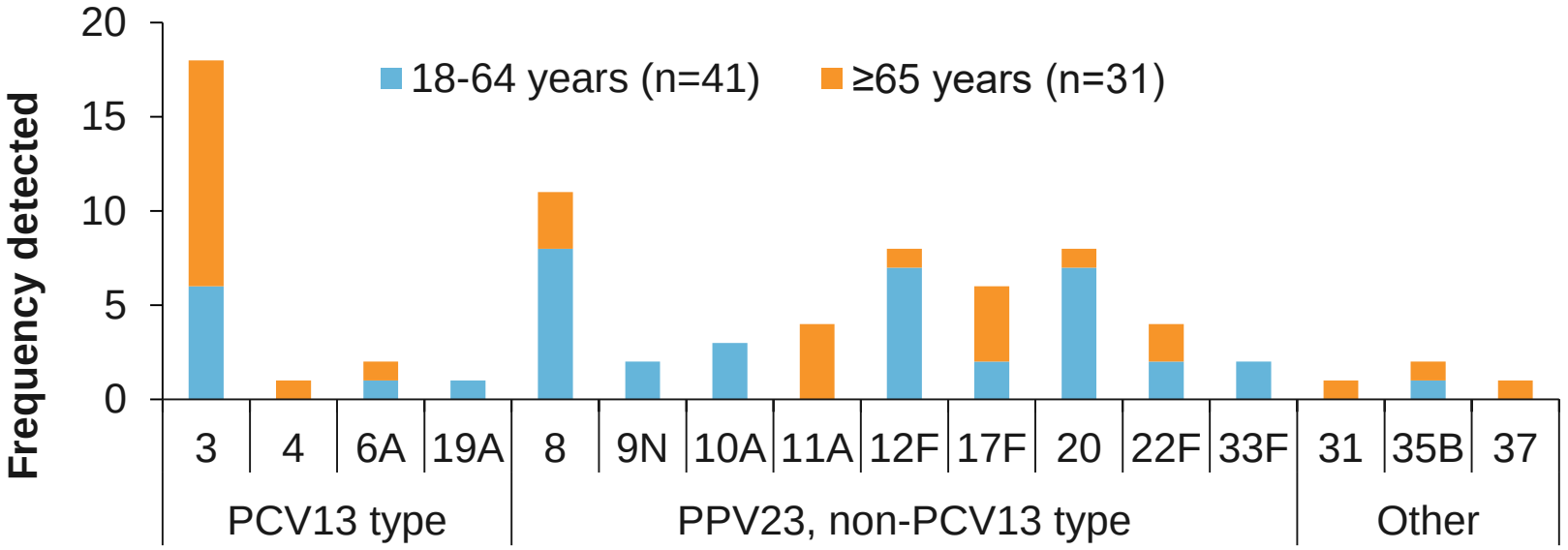
There was **100% serotype concordance** between SSUAD serotype and blood culture serotype.

Urine test results among CXR+ cases with any pneumococcal testing and community controls

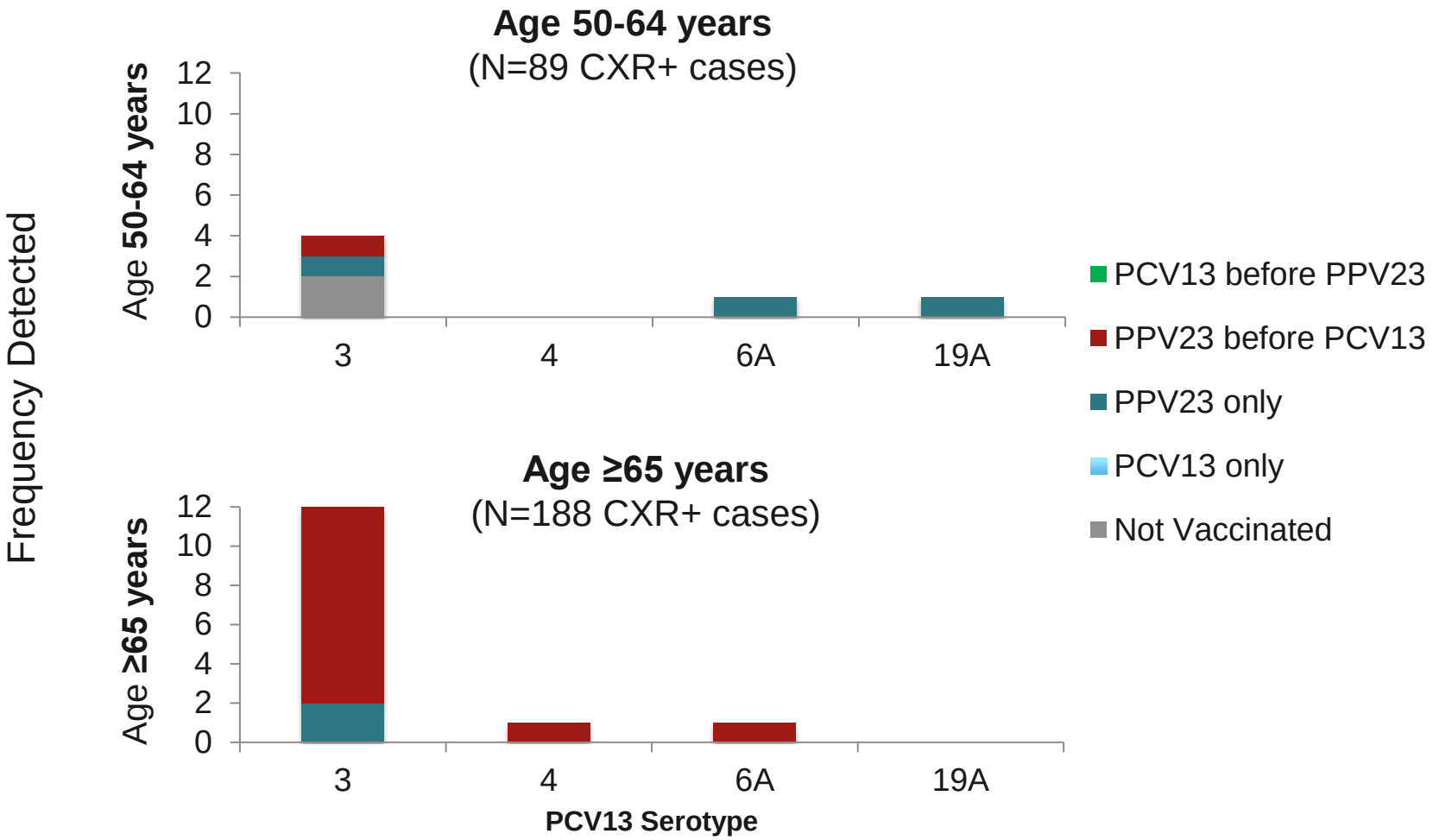
	Cases with ≥1 pneumococcal test			Controls		
	≥18 yrs N=348 n(%)	18-64 yrs N=166 n(%)	≥65 yrs N=182 n(%)	≥18 yrs N=249 n(%)	18-64 yrs N=116 n(%)	≥65 yrs N=133 n(%)
SSUAD+	68 (19.5)	40 (24.1)	28 (15.4)	7 (2.8)	5 (4.3)	2 (1.5)
BinaxNow+	54 (15.5)	25 (15.1)	29 (15.9)	8 (3.2)	2 (1.7)	6 (4.5)

Serotype results for CXR+ pneumococcal CAP

- Serotype data available in 72/91 (79%) pneumococcal cases
  - 22 (31%) were PCV13-type; excluding ST3, 4 (6%) were PCV13-type
    - 13 (62%) of 21 with vaccination status available had received PCV13 (all had received PPV23 first then PCV13)



PCV13 serotypes and vaccination status by age



Conclusions

- PCV13-type NP carriage in adults was very low prior to use of PCV13 in older adults and remains low
- Substantial indirect effects had been achieved by 2014-2015, leaving little opportunity to assess impact of PCV13 in ≥65 year olds on carriage or IPD
- Pneumococcus remains an important cause of CXR+ CAP among Native American adults
  - Non-PCV13 serotypes and serotype 3 predominated
  - SSUAD increased the detection of pneumococcal pneumonia over conventional methods but did not reveal an substantial burden of PCV13-type disease (except serotype 3) in the context of high PCV13 use in infants and ≥65 year olds

Acknowledgements

- Navajo, White Mountain Apache and Alaska Native communities and study participants
- CAIH Faculty and Staff
  - Kate O'Brien, Mathu Santosham, Ray Reid, Robert Weatherholtz, Lindsay Grant, Amanda Driscoll, Katie Trosclair, Grace Douglass
  - Field research team
- Navajo Nation IRB, Phoenix Area IHS IRB, JHSPH IRB
- White Mountain Apache Health Board and Tribal Council
- IHS Clinical and Lab partners
- New Mexico and Arizona Departments of Health
- Navajo Epidemiology Center
- Mike Jacobs – Case Western Reserve University
- Pfizer, Inc.
- CDC Arctic Investigations Program